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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,296	06/28/2004	Yuji Yamazaki	081356-0218	7715

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EXAMINER	
SKELDING, ZACHARY S	
ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,296	YAMAZAKI ET AL.	
	Examiner	Art Unit	
	ZACHARY SKELDING	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6 and 20-25* is/are pending in the application.

4a) Of the above claim(s) *1,2,4 and 6* is/are withdrawn from consideration.

5)☒ Claim(s) *20-22* is/are allowed.

6)☒ Claim(s) *23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks filed January 23, 2009 are acknowledged.

   Claims 20 has been amended.

   Claims 3, 5 and 7-19 have been canceled.

   Claims 1, 2, 4, 6 and 20-25 are pending.

   Claims 1, 2, 4 and 6 have been withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being directed to a non-elected Species.

   Claims 20-25 are under examination as they read on "anti-FGF-23 antibodies that bind amino acids 25-179 of SEQ ID NO:1".

2. This Office Action is in response to applicant's amendment and remarks filed January 23, 2009.

   The prior rejections of record can be found in the Office Action mailed July 24, 2008.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

   > A person shall be entitled to a patent unless –
   >
   > (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 23-25 stand rejected under 35 U.S.C. § 102(b) as anticipated by Itoh et al. (WO 01/66596, cited on applicant's IDS of June 28, 2004), as evidenced by Yu et al. (Endocrinology. 2005 Nov;146(11):4647-56) and Mohammadi et al. (Cytokine Growth Factor Rev. 2005 Apr;16(2):107-37), essentially for the reasons of record as put forth in the Office Action mailed July 24, 2008.

   Applicant argues in their remarks filed January 23, 2009, pages 4-5, that the claimed antibodies are not anticipated by Itoh for the following reasons:

   "Itoh prophesizes that antibodies, in principle, can be made from fragments of FGF-23, but there are no working examples to show that polyclonal or monoclonal antibodies, if produced as proposed, would have a given specificity or would recognize a given epitope. By contrast, the present application documents various monoclonal antibodies against FGF-23. Thus, Example 27 demonstrates that, among the antibodies tested, those produced by hybridomas FERM BP-7838 and FERM BP-7839 possess the activity of increasing phosphate in a mouse

model, while antibody produced by hybridoma FERM BP-7840 and antibody 2A2B fail to increase phosphate in the mouse. Accordingly, not all antibodies that can bind to FGF-23 have the activity of neutralizing the FGF-23 activity; hence, obtaining an antibody with such activity is not a necessary (i.e., an 'inherent') outcome of following the prophetic agenda for research that Itoh memorializes.

…however, it is impossible to test 'Itoh's antibodies' as a practical matter, since the reference actually fails to identify an actual antibody that might be tested for competitive binding. As a matter of law, moreover, the 'fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic.' MPEP § 2112, IV (original underscoring; citations omitted). 'In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art.' Id., quoting Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original).

The burden is with the examiner, therefore, to substantiate the proposition that Itoh necessarily places with the knowledgeable reader an antibody, per claim 23, that not only is 'competitive with the antibody produced by a [recited] hybridoma' but that also 'can neutralize ... FGF-23 activity.' Since not all anti-FGF-23 antibodies possess this activity, as applicants have shown, it follows that the examiner cannot rely on Itoh's general, prophetic disclosure to sustain his burden in this context."

Applicant's argument has been considered, but has not been found convincing, essentially for the reasons of record as put forth in the Office Action mailed July 24, 2008.

As stated in MPEP § 2112.01, "[w]here the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada,* 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)."

Itoh teaches that FGF-23 is proteolytically cleaved into two fragments, one of which comprises from amino acid 1 to around 179, that polyclonal or monoclonal antibodies can be generated against this fragment via "any suitable method known in the art…[f]or example, murine or human monoclonal antibodies can be produced by hybridoma technology…," and that said antibodies can be used for "preventing or treating diseases involving overexpression of the FGF-23 protein," such as "X-linked Hypophosphatemic rickets" (see Itoh page 18, 3rd to 4th paragraphs, page 30, 4th to 5th paragraphs and page 31, 3rd paragraph).

Thus, the prior art teaches antibodies that bind amino acids 1 to around 179 of SEQ ID NO: 1 and that block FGF-23 activity, for example in a bioassay (see Itoh, in particular page 30, 4th to 5th paragraphs and page 31, 1st-3rd paragraphs).

As stated in the previous Office Actions, given that the antibodies of Itoh bind amino acids 1 to around 179 of FGF-23, and given that the antibodies of Itoh, like the instantly claimed antibodies, can be used to treat hypophosphatemic diseases involving overexpression of FGF-23, such as X-linked Hypophosphatemic rickets, and further given the highly conserved receptor binding surface of the FGF molecules, including FGF-23, as evidenced by Wu and Mohammadi (described in greater detail in the Office Action of January 30, 2007), the antibodies of Itoh would inherently compete with the instantly claimed antibodies.

Applicant's argument that certain FGF-23 antibodies they have exemplified which bind SEQ ID NO: 1 fail to antagonize FGF-23 induced signaling does not negate the logic of the prima facie case of anticipation put forth in the previous Office Actions because the prima facie case of anticipation is based on the prior art antibodies both binding to amino acid residues 1-179 of FGF-23 AND antagonizing FGF-23 activity, and these are features of the anti-FGF-23 antibodies taught by Itoh.

Moreover, in contrast to applicant's argument, Itoh need not provide "working examples to show that polyclonal or monoclonal antibodies, if produced as proposed, would have a given specificity or would recognize a given epitope" or "...identify an actual antibody that might be tested for competitive binding." The disclosure of Itoh is sufficient to constructively reduce to practice monoclonal and polyclonal antibodies that bind amino acid residues 1-179 of FGF-23 and antagonize FGF-23 activity.

The burden is on applicant to put forth a convincing argument based on sound scientific reasoning and/or objective evidence that one of ordinary skill in the art, following the teachings of Itoh, would not necessarily produce antibodies and pharmaceutical compositions as claimed.

In conclusion, it is the Examiner's position that the instant Office Action and previous Office Actions have established a *prima facie* case of anticipation. The PTO has no reasonable ability to manufacture the antibodies of Itoh and determine whether there is, in fact, a patentable difference between the prior art product and the claimed product. It is applicant's burden to show that the reference antibodies are not competitive with the instantly claimed antibodies. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald* et al., 205 USPQ 594 (CCPA 1980).

Therefore, the instant claims stand rejected as anticipated by Itoh as evidenced by Yu and Mohammadi.

5. Claims 20-22 are allowable.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ZACHARY SKELDING whose telephone number is (571)272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Zachary Skelding
Patent Examiner
April 1, 2009

/Maher M. Haddad/
Primary Examiner,
Art Unit 1644